UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/721,091 | 11/26/2003 | Terry J. Amiss | P-6011 | 6187 |

46851 7590 03/22/2006

DAVID W. HIGHET
BECTON, DICKINSON AND COMPANY
1 BECTON DRIVE, MC110
FRANKLIN LAKES, NJ 07417

| EXAMINER | |
|---|---|
| VENCI, DAVID J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/721,091 | AMISS ET AL. | |
| | Examiner | Art Unit | |
| | David J. Venci | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *December 21, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *19-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-58* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 21, 2005 is entered.

Claims 19-58 are directed to non-elected inventions and were withdrawn from consideration in the Office Action of July 29, 2005.

Currently, claims 1-9 and 12-18 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 112***

Claims 1-9 and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step a), the recitation of "said fusion protein has a dissociation constant of at least 1 mM towards said analyte" is indefinite because the exact experimental conditions for measurement of dissociation constants is not clear. Applicants' specification does not provide a definite standard for ascertaining the dissociation constants, such that one of ordinary skill in the art would be reasonably apprised of the scope of the invention.

In claim 1, step a), the recitation of "said fusion protein has a dissociation constant of at least 1 mM towards said analyte" results in a scope mismatch in step c) wherein "said analyte is bound to said functional mutant periplasmic glucose-galactose binding protein".

In claim 1, step d), the recitation of "the measured the luminescence value" appears grammatically awkward.

In claim 18, the recitation of proprietary trademarks (e.g. "Alexa") is indefinite.

***Claim Rejections - 35 USC § 103***

Claims 1-9, 12-13 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga & Looger (US 2004/0118681) in view of Romoser *et al.*, 272 J. BIOL. CHEM. 13270 (1997).

Hellinga & Looger teach a method for quantifying an analyte (see para. [0031], "[a]ssays for ligand") in a sample (see para. [0031], "body fluids") comprising the steps of:

a) administering a fusion protein (see para. [0029], "the reporter group can be present as a fusion"; para. [0030], "gene fusions") to said sample, said fusion protein comprising a functional periplasmic binding protein (see Table 5, "glucose BP");

b) measuring the luminescence of said fluorescent fusion protein in the absence of analyte (see para. [0031], "[a] blank sample containing no ligand");

c) measuring the luminescence of said fluorescent fusion protein in the presence of analyte (see para. [0031], "[a]ssays for ligand"); and

Hellinga & Looger do not describe a detection scheme based on resonance energy transfer incorporating a "labeling moiety" and "fluorescent protein".

However, Romoser *et al.* describe a detection scheme based on resonance energy transfer (see Abstract, "fluorescence resonance energy transfer between the two fluorophores") incorporating a labeling moiety and fluorescent protein (see Title, "Two Green Fluorescent Protein Variants").

It would have been obvious to a person of ordinary skill in the art to replace the detection scheme of Hellinga & Looger with a detection scheme based on resonance energy transfer between a labeling moiety and fluorescent protein because Romoser *et al.* discovered that such a detection scheme resulted in a 30% fractional reduction at $F_{510}$ *in vivo* and a 65% fractional reduction at $F_{510}$ *in vitro* (see p. 13273, right column, first full paragraph).

---

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga & Looger (US 2004/0118681) and Romoser *et al.*, 272 J. BIOL. CHEM. 13270 (1997), as applied to claims 1 and 13, and further in view of Tsien & Campbell (US 2003/0059835).

Hellinga & Looger and Romoser *et al.* teach a method for quantifying an analyte as substantially described, *supra*, and incorporated herein.

Lakowicz *et al.* do not teach a method using DsRed2(C119A).

However, Tsien & Campbell teach the use of DsRed2 (see para. [0012]), including C119 mutant DsRed (see e.g. para. [0128], "C117E"), for use as a member of a donor/acceptor pair for fluorescence resonance energy transfer (see para. [0008]).

It would have been obvious for a person of ordinary skill in the art to modify the method of Hellinga & Looger and Romoser *et al.* by using DsRed2(C119A) because Tsien & Campbell discovered the importance of C119 in fluorescent protein oligomerization. Tsien & Campbell also discovered that, by mutating key amino acid residues—including C119—oligomerization can be minimized (see e.g. para. [0128], "The ultimate product of the mutagensis approach described herein is a monomeric red fluorescent protein"), which results in improved data interpretation (see para. [0010] – [0013]).

***Response to Arguments***

In prior Office Action, claims 1-13 and 17-18 were rejected under 35 U.S.C. 102(b) as being anticipated by Lakowicz et al. (US 6,197,534). In addition, claims 14-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lakowicz et al. (US 6,197,534) in view of Tsien & Campbell (US 2003/0059835). Applicants' amendment and argumentation are fully persuasive and sufficient to overcome these rejections. Accordingly, these rejections are withdrawn.

In prior Office Action, claims 1-9, 12-13 and 17-18 were provisionally rejected under the doctrine of obviousness-type double patenting in view of copending Application No. 10/776,643 and Lakowicz et al. (US 6,197,534). In addition, claims 14-16 were provisionally rejected under the doctrine of obviousness-type double patenting in view of copending Application No. 10/776,643, and Lakowicz et al. (US 6,197,534) and Tsien & Campbell (US 2003/0059835). Applicants' amendment is fully persuasive and sufficient to overcome these rejections. Accordingly, these rejections are withdrawn.

***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
3/20/06